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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,177	11/25/2003	Jun Nakamura	US-110	6388

38108 7590 03/05/2007

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EXAMINER	
RAMIREZ, DELIA M	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/720,177	NAKAMURA ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5 and 7-19* is/are pending in the application.

4a) Of the above claim(s) *8-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7 and 12-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: alignments

DETAILED ACTION

Status of the Application

Claims 1, 4-5, 7-19 are pending.

Applicant's amendment of claims 1, 4-5, 7, cancellation of claims 2-3, 6, and addition of claims 12-19 as submitted in a communication filed on 12/8/2006 is acknowledged.

As indicated in the Non Final action mailed on 9/12/2006, claims 8-11 were withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to an invention non-elected with traverse in a communication filed on 6/30/2006.

New claims 12-19 are deemed directed to the elected subject matter (i.e., bacterium modified to reduce glutaminase activity) and find support in the specification, pages 8, 12, 13 and 14. Claims 1, 4-5, 7, 12-19 are at issue and are being examined herein.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

1. Claims 1, 5, and 16 are objected to due to the recitation of "DNA which is able to hybridize with the DNA sequence". As known in the art, hybridization occurs among nucleic acid molecules. A nucleotide sequence is a graphical representation of the order in which nucleotides are arranged in a nucleic acid molecule. Therefore, hybridization cannot occur between a DNA and a sequence. It is suggested the term be amended by deleting the term "sequence". Appropriate correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1, 4-5, 7 remain rejected and new claims 12-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

4. This rejection has been discussed at length in the Non Final action mailed on 9/12/2006 and it is applied to new claims 12-19 for the reasons of record and those set forth below.

5. Applicant argues that the claims have been amended (1) to specifically recite how to reduce glutaminase activity, (2) to provide an upper limit of activity, (3) to recite a specific sequence which is being disrupted/mutated or enhanced, and (4) to recite specific hybridization conditions. Applicant submits that one of skill in the art can obtain the claimed bacteria without further description of particular species of glutaminase genes. Thus, the claimed invention is adequately described.

6. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection or avoid the rejection of new claims 12-19. The amendments made to the claims are acknowledged. However, the amendments made are not sufficient for one of skill in the art to conclude that the disclosure adequately describes the full scope of the claimed invention. The instant claims encompass a coryneform bacterium modified (a) to reduce glutaminase activity in said bacterium by mutating any region of a glutaminase gene comprising SEQ ID NO: 1 or a structural homolog thereof, and (b) to increase glutamine synthetase activity in said bacterium by (i) increasing the expression of a glutamine synthetase gene comprising SEQ ID NO: 3, or a structural homolog thereof, using any method, or (ii) any modification in the expression regulatory region of a gene comprising SEQ ID NO: 3 or a structural homolog thereof, such that the modifications of (a)-(b) would result in a reduction of glutaminase activity to 0.1/0.01 U/mg protein and/or a ratio of glutamine synthetase activity to glutaminase activity of 2 to 1. Thus, the claims require, for example, unknown modifications in the transcription control region or coding region of the recited gene which would result in a glutaminase having an enzymatic activity of 0.1 or 0.01 U/mg of protein. While the specification discloses that a deletion in the gene of SEQ ID NO: 1 would result in a severe reduction in glutaminase activity, the

specification is completely silent with regard to the specific mutations in the regulatory region of the gene of SEQ ID NO: 1 which would result in the recited glutaminase activity levels, or the specific mutations in the regulatory/coding region of a structural homolog of the gene of SEQ ID NO: 1 which would reduce glutaminase activity to the required levels. In addition, the specification is completely silent with regard to the modifications required in any coryneform bacterium such that the recited ratio of glutaminase to glutamine synthetase activity can be achieved. Also, while the claims require (1) any modification which would increase the expression of the glutamine synthetase gene of SEQ ID NO: 3, or the structural homolog recited, or (2) any modification in the expression regulatory region of the glutamine synthetase gene of SEQ ID NO: 3, or the structural homolog recited, to increase enzymatic activity, the specification is completely silent with regard to additional methods to increase expression or enzymatic activity beyond using strong heterologous promoters or increasing the copy number of the gene encoding the enzyme. The claims encompass, for example, the addition of compounds (chemicals and proteins) which would induce transcription and mutations in the regulatory region of a gene to increase transcription. However, the specification fails to disclose the structure of any compound which would induce transcription, or the specific structural modifications required in the regulatory region of a gene which would increase expression such that the specific enzymatic levels/ratios recited can be achieved. The specification discloses one single modification to inactivate the glutaminase gene of SEQ ID NO: 1 such that the recited enzymatic activity levels can be achieved, and two modifications to increase the enzymatic activity of the glutamine synthetase gene of SEQ ID NO: 3 (i.e., strong heterologous promoter and increase in copy number). Thus, for the reasons extensively discussed in the Non Final action mailed on 9/12/2006, and those set forth above, one cannot reasonably conclude that the claimed invention is adequately described by the teachings of the specification.

7. Claims 1, 4-5, 7 remain rejected and new claims 12-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *C. glutamicum* cell wherein said cell has been modified to reduce glutaminase activity and to increase glutamine synthetase activity, wherein the reduction in glutaminase activity is due to an inactivating deletion in the *C. glutamicum* glutaminase gene of SEQ ID NO: 1, and the increase in glutaminase activity is due to (i) an increase in the copy number of the *C. glutamicum* glnA gene, or (ii) an increase in expression of the *C. glutamicum* glnA gene by placing said gene under the control of a heterologous promoter, does not reasonably provide enablement for (1) a coryneform bacterium modified (i) to reduce glutaminase activity in said bacterium by mutating any region of a glutaminase gene comprising SEQ ID NO: 1 or a structural homolog thereof, and/or (ii) to increase glutamine synthetase activity in said bacterium by increasing the expression of a glutamine synthetase gene comprising SEQ ID NO: 3, or a structural homolog thereof, or by any modification in the expression regulatory region of a gene comprising SEQ ID NO: 3 or a structural homolog thereof, such that the modifications of (i)-(ii) would result in a reduction of glutaminase activity to 0.1/0.01 U/mg protein and/or a ratio of glutamine synthetase activity to glutaminase activity of 2 to 1, or (2) a genus of DNAs encoding a glutaminase or a glutamine synthetase, wherein said DNAs hybridize under the recited conditions to the polynucleotides of SEQ ID NO: 1 or 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

8. This rejection has been discussed at length in the Non Final action mailed on 9/12/2006 and it is applied to new claims 12-19 for the reasons of record and those set forth below.

9. Applicant argues that the claims have been amended (1) to specifically recite how to reduce glutaminase activity, (2) to provide an upper limit of activity, (3) to recite a specific sequence which is being disrupted/mutated or enhanced, and (4) to recite specific hybridization conditions. Applicant submits that disrupting or mutating a gene on a bacterial chromosome is well known in the art and that

those species not exemplified in the specification can be easily obtained by the person of ordinary skill in the art. Thus, the claimed invention is fully enabled by the disclosure.

10. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection or avoid the rejection of new claims 12-19. The Examiner acknowledges the amendments to the claim. However, the Examiner disagrees with Applicant's contention that the teachings of the specification enable the full scope of the claims. The instant claims encompass a coryneform bacterium modified (a) to reduce glutaminase activity in said bacterium by mutating any region of a glutaminase gene comprising SEQ ID NO: 1 or a structural homolog thereof, and (b) to increase glutamine synthetase activity in said bacterium by (i) increasing the expression of a glutamine synthetase gene comprising SEQ ID NO: 3, or a structural homolog thereof, using any method, or (ii) any modification in the expression regulatory region of a gene comprising SEQ ID NO: 3 or a structural homolog thereof, such that the modifications of (a)-(b) would result in a reduction of glutaminase activity to 0.1/0.01 U/mg protein and/or a ratio of glutamine synthetase activity to glutaminase activity of 2 to 1. As written, the claims require unknown modifications in the transcription control region or coding region of the recited gene which would result in a glutaminase having an enzymatic activity of 0.1 or 0.01 U/mg of protein. While the specification discloses that a deletion in the gene of SEQ ID NO: 1 results in reduction of glutaminase activity, the specification fails to disclose (1) the specific mutations in the regulatory region of the gene of SEQ ID NO: 1 which would result in the recited glutaminase activity levels, (2) the specific mutations in the regulatory/coding region of a structural homolog of the gene of SEQ ID NO: 1 which would reduce glutaminase activity to the required levels, or (3) the modifications required in any coryneform bacterium such that the recited ratio of glutaminase to glutamine synthetase activity can be achieved. Also, the claims require (1) any modification which would increase the expression of the glutamine synthetase gene of SEQ ID NO: 3, or the structural homolog recited, or (2) any modification in the expression regulatory region of the glutamine synthetase gene of SEQ ID NO: 3,

or the structural homolog recited, to increase enzymatic activity. However, the specification provides no information with regard to additional methods to increase expression of a gene or enzymatic activity, such as the identity and structure of any chemical/protein which would induce transcription, or the specific structural modifications required in the regulatory region of a gene to increase expression such that the specific enzymatic levels/ratios recited can be achieved. In view of the fact that neither the specification nor the art provide any guidance as to the structural modifications and/or compounds which would result in the recited genes to express the corresponding enzymes at the recited enzymatic activity levels, one of skill in the art would have to go through the burden of undue experimentation to determine (1) all the structural modifications in the gene of SEQ ID NO: 1, or a structural homolog as recited, which would result in a glutaminase activity of 0.1 or 0.01 U/mg protein, (2) all the structural modifications in the regulatory gene of SEQ ID NO: 3, or a structural homolog as recited, which would result in a glutamine synthetase activity that is double that of glutaminase, or (3) all the compounds which would enhance transcription of any glutamine synthetase gene that hybridize under the conditions recited to the gene of SEQ ID NO: 3 such that the enzymatic activity of the protein encoded by said gene is double that of glutaminase.

The claims also require an extremely large genus of structural homologs of the genes of SEQ ID NO: 1 and 3 which hybridize under the recited conditions to the nucleic acids of SEQ ID NO: 1 and 3. A calculation of the Tm of the polynucleotides recited in claims 1, 5, 16 shows that under the hybridization conditions recited, the recited polynucleotides can be approximately 69.8% sequence identical to the polynucleotides of SEQ ID NO: 1 or 3. Using the well known equation of Meinkoth and Wahl (Current Protocols in Molecular Biology, Hybridization Analysis of DNA Blots, pages 2.10.8-2.10.11, 1993), Tm = 81.5 °C +16.6x$\log_{10}$[Na+] +0.41x(%GC) - .61x(%form) – 500/L), the corresponding Tm for the polynucleotides recited is approximately 90.2 °C assuming a G+C content of 50% and neglecting the term 500/L since L (length of polynucleotide) is over 2000 nucleotides (90.2 °C = 81.5 + 16.6x$\log_{10}$[3.9/20]

+0.41x(%50) - .61(%form = 0); for 20xSSC the molar concentration of Na+ is 3.9). As known in the art, Tm is reduced by approximately 1 °C for each 1% mismatching, therefore under the conditions recited (1xSSC and 60 °C), a wash at 60 °C is equivalent to approximately 30.2% mismatching (30.2% = 90.2°C – 60°C). This level of mismatching amounts to 635-755 nucleotides which can be modified (635 = 0.302x2100; 755 = 0.302x2500) within SEQ ID NO: 1 and 3. The total number of variants of a polynucleotide having a specific sequence identity can be calculated from the formula $N!x3^{A}/(N-A)!/A!$, where N is the length in nucleotides of the reference polynucleotide and A is the number of allowed substitutions for a specific % identity. Thus, for a variant of the polynucleotide of SEQ ID NO: 1 having 69.8% sequence identity to SEQ ID NO: 1, the total number of variants to be tested is $2100!x3^{635}/(2100-635)!/635!$ (SEQ ID NO: 1 has 2100 nucleotides) or $1.58x10^{860}$ variants. The number of variants to be tested for a homolog of the polynucleotide of SEQ ID NO: 3 as recited is even greater since SEQ ID NO: 3 has 2500 nucleotides. In addition to the fact that the claims encompass an extremely large genus of polynucleotides, it is noted that the genus of polynucleotides recited can potentially encompass polynucleotides encoding proteins having little or no structural homology to the polypeptides of SEQ ID NO: 2 or 4 since the 635-755 mismatches in the polynucleotides of SEQ ID NO: 1 or 3 can potentially alter all/most codons.

As previously indicated in the Non Final action mailed on 9/12/2006, neither the specification nor the art provides any teaching or guidance as to a structure/function correlation which would allow one of skill in the art to envision the structure of any nucleic acid encoding a glutaminase or a glutamine synthetase. The specification is also silent with regard to the structural elements in the polynucleotides of SEQ ID NO: 1 or 3 which are essential in any variant to encode a glutaminase or a glutamine synthetase. The art as extensively discussed in the Non Final action clearly teaches the unpredictability of the art in regard to determining function based solely on structural homology. Thus, while the claims require an extremely large genus of nucleic acids, the specification is completely silent with regard to the structural

features of those species most likely to encode proteins having the recited enzymatic activity. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. Therefore, for the reasons extensively discussed in the Non Final action mailed on 9/12/2006, and those set forth above, one cannot reasonably conclude that the full scope of the claimed invention is enabled by the teachings of the specification and those of the prior art.

Claim Rejections - 35 USC § 103

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 1, 5, 7 remain rejected and claims 4, 13, 14, 15, 16, 17, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura et al. (EP 1229121 A2 published 8/7/2002; cited in the IDS) in view of Pompejus et al. (WO 01/00843, published 1/4/2001; cited in the IDS) and further in view of Duran et al. (Microbiology 141:2883-2889, 1995).

13. This rejection has been extensively discussed in the Non Final action mailed on 9/12/2006. However, the subject matter of previously presented claims 3 and amended claim 4 was not included in this rejection as previously stated. Upon further consideration, the invention of previously presented claim 3 and amended claim 4 is considered obvious over the instant references for the following reasons.

14. Nakamura et al. teach a method for producing L-glutamine by fermentation of an L-glutamine producing *C. glutamicum* cell, wherein said cell has been modified to increase the intracellular concentration of glutamine synthetase by increasing the copy number of the glnA gene of *C. glutamicum* (encodes glutamine synthetase; Example 1, Table 1, strain AJ12418/pGS). Nakamura et al. also teach a method for production of L-glutamine and suppression of L-glutamic acid as a by-product (paragraph

[005]-[006]). Nakamura et al. do not teach a method for producing L-glutamine wherein glutaminase activity is reduced. Duran et al. teach that glutaminase degrades glutamine to yield glutamate and ammonium (page 2884, left column, first full paragraph) and disclose a mutant *R. etli* (LM16) wherein the chromosomal glutaminase gene is disrupted by Tn5 mutagenesis (Page 2884, Methods, Strains and plasmid). The reference also teaches that LM16 produces more glutamine than glutamate when cultured with different substrates (page 2886, Table 1). As shown in Table 1, the amount of glutamine produced varies from 53X (49/0.9) to 2X (0.8/04) more glutamine in the glutaminase deficient mutant LM16 as compared to the wild type *R. etli*. Duran et al. do not teach a *C. glutamicum* or coryneform bacterium deficient in glutaminase. Pompejus et al. teach *C. glutamicum* genes encoding glutaminase and glutamine synthetase (Table 1, page 56, Glutamate and Glutamine metabolism, RXA00335 and RXN03176; SEQ ID NO: 97-98 (glutamine synthetase) and SEQ ID NO: 101-102 (glutaminase)). The glutaminase gene of Pompejus et al. (SEQ ID NO: 101 in Pompejus et al.) is 99% sequence identical to nucleotides 827-1687 of SEQ ID NO: 1 (99% = 851x100/861; see attached alignment), thus it would be expected that the glutaminase gene of Pompejus et al. would hybridize to the polynucleotide of SEQ ID NO: 1 of the instant application at the conditions recited. The glutamine synthetase gene of Pompejus et al. (SEQ ID NO: 97 in Pompejus et al.) is 99.5% sequence identical to the polynucleotide of SEQ ID NO: 3 (99.5% = 1547x100/1554; see attached alignment), thus it would be expected that the glutamine synthetase gene of Pompejus et al. would hybridize to the polynucleotide of SEQ ID NO: 3 of the instant application at the conditions recited. Pompejus et al. also teach that the disclosed *C. glutamicum* genes can be used for the modulation of production of amino acids (page 11, lines 20-25) and that glutamine is used in both pharmaceutical and cosmetics industries (page 13, lines 17-19). Pompejus et al. do not teach a mutant coryneform bacterium wherein the glutaminase activity in said bacterium has been reduced and the glutamine synthetase activity has been enhanced.

Claims 1, 4, 5, 7, 13-17 and 19 are directed in part to a coryneform bacterium that produces L-glutamine modified such that (1) the glutaminase activity of said bacterium is reduced by disrupting the glutaminase gene on the chromosome, and the glutamine synthetase activity in said bacterium is increased by increasing the copy number of the gene encoding said glutamine synthetase or by placing said gene under the control of the lac, trp, or trc promoter, wherein the glutaminase gene to be disrupted hybridizes under the stringent conditions recited to the polynucleotide of SEQ ID NO: 1 and the glutamine synthetase gene hybridizes under the stringent conditions recited to the polynucleotide of SEQ ID NO: 3, wherein the glutamine synthetase activity in said bacterium is at least double that of the glutaminase activity, and wherein said glutaminase activity is 0.01 U/mg protein or less.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify a *C. glutamicum* cell that comprises the *C. glutamicum* glutaminase gene of Pompejus et al. by (1) deleting all or most of the coding region of the glutaminase gene, and (2) increasing the expression of the *C. glutamicum* glutamine synthetase gene of Pompejus et al. either by increasing its copy number or by placing said gene under the control of the lac, trp, or trc promoters. A person of ordinary skill in the art is motivated to construct such *C. glutamicum* cell in view of the fact that (1) Duran et al. teach an increase in L-glutamine production when the glutaminase gene is disrupted, (2) Pompejus et al. teach that L-glutamine is a chemical used in the pharmaceutical and cosmetics industries, (3) Duran et al. teach that glutaminase degrades L-glutamine to glutamate, (4) Nakamura et al. teach a method for the production of L-glutamine where a reduction in the production of L-glutamic acid is desired, (5) Nakamura et al. teach that increasing glutamine synthetase activity results in an increase in L-glutamine production, and (6) the use of strong heterologous promoters allows for controlled expression of the protein of interest as they require the presence of inducers for expression to occur (e.g., lactose and tryptophan).

One of ordinary skill in the art has a reasonable expectation of success at modifying such *C. glutamicum* cell in view of the fact that Pompejus et al. teach the *C. glutamicum* glutaminase and

glutamine synthetase genes, inactivation of genes by deletion if the sequence of the target gene is known is well known and widely practiced in the art, Nakamura et al. teach increased expression of the glutamine synthetase gene for increased L-glutamine production in *C. glutamicum*, Duran et al. teach that inactivation of the glutaminase gene results in increased L-glutamine production, and increased expression by increasing the copy number of the gene of interest and the use of lac, trc, or trp promoters is well known in the art. In the absence evidence to the contrary, if no additional sources of glutaminase activity are present, a deletion of the glutaminase gene wherein most or all of the coding region is removed would result in no glutaminase activity (i.e., 0 U/mg protein). If the glutaminase activity is 0 U/mg protein, then the glutamine synthetase activity would be expected to be at least double that of glutaminase. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

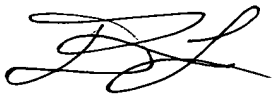
Conclusion

15. No claim is in condition for allowance.

16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571)

272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



Delia M. Ramirez, Ph.D.
Primary Patent Examiner
Art Unit 1652

DR
February 28, 2007

SEQ ID NO: 1

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Db       1081 ATTCAAACAGCTTTCCGACGACATGGGCCTCCACCTCATGTCCACCGAGCAGGTATCCGG 1140

Qy       1699 CCACGCAGTACGATCCATTACGCGGGACGGCGACACCACCTTCATCCAAATGCAGGGCGC 1758
              |||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||
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Qy       1759 CATGAACTTCTCAGCCAGCGAAAGCTTCCTCCACGCCATCGTGGAACACAACTTTGAAGG 1818
              |||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||
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Qy       1819 CACCGAAGTTGTTCTTGATCTCACCCGAGTACTTAGCTTCCACCCCGTAGCCATCCGCAT 1878
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 CACCGAAGTTGTTCTTGATCTCACCCGAGTACTTAGCTTCCACCCCGTAGCCATCCGCAT 1320

Qy       1879 GATCAAAGAAGGCCTCAAACGCATCCGCGACGCAGGCTTTGAGGTGTTCATCCTCGACCC 1938
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 GATCAAAGAAGGCCTCAAACGCATCCGCGACGCAGGCTTTGAGGTGTTCATCCTCGACCC 1380

Qy       1939 AGATGACGTACTGCCCGATTTCATGTTTTCCGACGGCACCATCTGCAAAGAACGAGTGTG 1998
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 AGATGACGTACTGCCCGATTTCATGTTTTCCGACGGCACCATCTGCAAAGAACGAGTGTG 1440

Qy       1999 ACCGGTAGCTTTATGGTCTGAACAATTC 2026
              |||||||||||||||| ||||||||||||
Db       1441 ACCGGTAGCTTTATGGGCTGAACAATTC 1468
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RESULT 5
AAF71803
ID   AAF71803 standard; DNA; 861 BP.
XX
AC   AAF71803;
XX
DT   30-APR-2001  (first entry)
XX
DE   Corynebacterium glutamicum MP protein nucleotide sequence SEQ ID NO:101.
XX
KW   Corynebacterium glutamicum; metabolic pathway protein; MP protein;
KW   fine chemical production; microorganism; organic acid; nucleoside;
KW   nonproteinogenic amino acid; purine base; pyrimidine base; nucleotide;
KW   lipid; saturated fatty acid; unsaturated fatty acid; diol; vitamin;
KW   carbohydrate; aromatic compound; cofactor; polyketide; enzyme; ds.
XX
OS   Corynebacterium glutamicum.
XX
PN   WO200100843-A2.
XX
PD   04-JAN-2001.
XX
PF   23-JUN-2000; 2000WO-IB000923.
XX
PR   25-JUN-1999;   99US-0141031P.
PR   01-JUL-1999;   99DE-01030476.
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PR   08-JUL-1999;   99DE-01031541.
PR   08-JUL-1999;   99DE-01031573.
PR   08-JUL-1999;   99DE-01031592.
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PR   09-JUL-1999;   99DE-01032227.
PR   09-JUL-1999;   99DE-01032228.
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PR   09-JUL-1999;   99DE-01032230.
PR   14-JUL-1999;   99DE-01032922.
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PR   14-JUL-1999;   99DE-01032928.
PR   14-JUL-1999;   99DE-01033004.
PR   14-JUL-1999;   99DE-01033005.
PR   14-JUL-1999;   99DE-01033006.
PR   12-AUG-1999;   99US-0148613P.
PR   27-AUG-1999;   99DE-01040764.
PR   27-AUG-1999;   99DE-01040765.
PR   27-AUG-1999;   99DE-01040766.
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PR   31-AUG-1999;   99DE-01041378.
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PR   31-AUG-1999;   99DE-01041394.
PR   31-AUG-1999;   99DE-01041396.
PR   03-SEP-1999;   99DE-01042076.
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PR   03-SEP-1999;   99DE-01042095.
PR   03-SEP-1999;   99DE-01042124.
PR   03-SEP-1999;   99DE-01042129.
PR   09-MAR-2000; 2000US-0187970P.
XX
PA   (BADI ) BASF AG.
XX
PI   Pompejus M,  Kroeger B,  Schroeder H,  Zelder O,  Haberhauer G;
XX
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SEQ ID NO:1

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DR   WPI; 2001-137957/14.
DR   P-PSDB; AAB79684.
XX
PT   Nucleic acids from Corynebacterium glutamicum encoding metabolic pathway
PT   proteins, useful for producing fine chemicals in microorganisms,
PT   including organic acids, nonproteinogenic amino acids, and purine and
PT   pyrimidine bases.
XX
PS   Claim 3; Page 314-315; 1737pp; English.
XX
CC   AAF71753 to AAF72330 encode the Corynebacterium glutamicum metabolic
CC   pathway (MP) proteins given in AAB79634 to AAB80211. The C. glutamicum MP
CC   nucleic acids are useful for the production of fine chemicals in
CC   microorganisms, including organic acids, nonproteinogenic amino acids,
CC   purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated
CC   and unsaturated fatty acids, diols, carbohydrates, aromatic compounds,
CC   vitamins, cofactors, polyketides and enzymes
XX
SQ   Sequence 861 BP; 199 A; 309 C; 205 G; 148 T; 0 U; 0 Other;

  Query Match             40.2%;  Score 845;  DB 4;  Length 861;
  Best Local Similarity   98.8%;  Pred. No. 3.4e-214;
  Matches  851;  Conservative    0;  Mismatches   10;  Indels    0;  Gaps    0;

Qy        827 GAGTTGGCCGATTACATCCCGGAACTAAAATCTGCCGACCCAAACCCGCTGGCAGTAGCC 886
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Db          1 GAGTTGGCCGATTACATCCCGGAACTAAAATCTGCGGACCCAAACCCGCTGGCAGTAGCC 60

Qy        887 CTGTGCACCGTTAACGGACACATCTACAGCGCAGGCGATGACGACATCGAATTCACCATG 946
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Db        121 CAAAGTATTTCCAAGCCATTTGCCTACGCACTCGCACTCCAAGAATGCGGCTTTGATGAG 180

Qy       1007 GTCTCTGCATCCGTGGCCTTGGAACCCTCCGGTGAGGCCTTCAACGAACTTTCCCTCGAC 1066
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Qy       1067 GGCGAAAACCGCCCCATGAACCCCATGATCAACGCCGGCGCGATCGCCATCAACCAGCTG 1126
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Qy       1667 CTCCACCTTATGTCCACCGAG 1687
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Db        841 CTCCACCTCATGTCCACCGAG 861
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RESULT 6
AAF71804
ID   AAF71804 standard; DNA; 861 BP.
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AC   AAF71804;
XX
DT   30-APR-2001  (first entry)
XX
DE   Corynebacterium glutamicum MP protein nucleotide sequence SEQ ID NO:103.
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KW   Corynebacterium glutamicum; metabolic pathway protein; MP protein;
KW   fine chemical production; microorganism; organic acid; nucleoside;
KW   nonproteinogenic amino acid; purine base; pyrimidine base; nucleotide;
KW   lipid; saturated fatty acid; unsaturated fatty acid; diol; vitamin;
KW   carbohydrate; aromatic compound; cofactor; polyketide; enzyme; ds.
XX
OS   Corynebacterium glutamicum.
XX
PN   WO200100843-A2.
XX
PD   04-JAN-2001.
XX
PF   23-JUN-2000; 2000WO-IB000923.
XX
PR   25-JUN-1999;   99US-0141031P.
PR   01-JUL-1999;   99DE-01030476.
PR   02-JUL-1999;   99US-0142101P.
PR   08-JUL-1999;   99DE-01031415.
PR   08-JUL-1999;   99DE-01031418.
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SEQ ID NO: 3

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Qy        2161 CAGGAAGACACCGACTTCCTCACCGAGTCTGACGTCTTCACCGAGGATCTCATCGAGGCG 2220
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Qy        2221 TACATCCAGTACAAGTACGACAACGAGATCTCCCCAGTTCGCCTGCGCCCAACCCCGCAG 2280
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RESULT 3
AAF71801
ID   AAF71801 standard; DNA; 1554 BP.
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AC   AAF71801;
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DT   30-APR-2001  (first entry)
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DE   Corynebacterium glutamicum MP protein nucleotide sequence SEQ ID NO:97.
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KW   Corynebacterium glutamicum; metabolic pathway protein; MP protein;
KW   fine chemical production; microorganism; organic acid; nucleoside;
KW   nonproteinogenic amino acid; purine base; pyrimidine base; nucleotide;
KW   lipid; saturated fatty acid; unsaturated fatty acid; diol; vitamin;
KW   carbohydrate; aromatic compound; cofactor; polyketide; enzyme; ds.
XX
OS   Corynebacterium glutamicum.
XX
PN   WO200100843-A2.
XX
PD   04-JAN-2001.
XX
PF   23-JUN-2000; 2000WO-IB000923.
XX
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PR   08-JUL-1999;   99DE-01031415.
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PR   31-AUG-1999;   99DE-01041394.
PR   31-AUG-1999;   99DE-01041396.
PR   03-SEP-1999;   99DE-01042076.
PR   03-SEP-1999;   99DE-01042077.
PR   03-SEP-1999;   99DE-01042079.
PR   03-SEP-1999;   99DE-01042086.
PR   03-SEP-1999;   99DE-01042087.
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PR   03-SEP-1999;   99DE-01042095.
PR   03-SEP-1999;   99DE-01042124.
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PR 03-SEP-1999; 99DE-01042129.
PR 09-MAR-2000; 2000US-0187970P.
XX
PA (BADI) BASF AG.
XX
PI Pompejus M, Kroeger B, Schroeder H, Zelder O, Haberhauer G;
XX
DR WPI; 2001-137957/14.
DR P-PSDB; AAB79682.
XX
PT Nucleic acids from Corynebacterium glutamicum encoding metabolic pathway
PT proteins, useful for producing fine chemicals in microorganisms,
PT including organic acids, nonproteinogenic amino acids, and purine and
PT pyrimidine bases.
XX
PS Claim 3; Page 301-303; 1737pp; English.
XX
CC AAF71753 to AAF72330 encode the Corynebacterium glutamicum metabolic
CC pathway (MP) proteins given in AAB79634 to AAB80211. The C. glutamicum MP
CC nucleic acids are useful for the production of fine chemicals in
CC microorganisms, including organic acids, nonproteinogenic amino acids,
CC purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated
CC and unsaturated fatty acids, diols, carbohydrates, aromatic compounds,
CC vitamins, cofactors, polyketides and enzymes
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SQ Sequence 1554 BP; 385 A; 520 C; 356 G; 293 T; 0 U; 0 Other;

Query Match 61.7%; Score 1542.8; DB 4; Length 1554;
Best Local Similarity 99.5%; Pred. No. 0;
Matches 1547; Conservative 0; Mismatches 7; Indels 0; Gaps 0;

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Db          1 ACTACATTTGCAGCCAAGTCTACTACTTGATCTTCAAAGGTCAGCAATTGTGAACAAAGC 60

Qy        834 TACAAATAAACCGTTCCACCCATGTCAATGAGGAGTCACCGTGGCGTTTGAAACCCCGGA 893
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Db         61 TACAAATAAACCGTTCCGCCCATGTCAATGAGGAGTCACCGTGGCGTTTGAAACCCCGGA 120

Qy        894 AGAAATTGTCAAGTTCATCAAGGATGAAAACGTCGAGTTCGTTGACGTTCGATTCACCGA 953
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Qy       1074 TGACATGAATCTCCTGCCAGACCTCGGAACGGCCACCCTTGATCCATTCCGCAAGGCAAA 1133
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SEQ ID NO: 3

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Qy       2034 CGACGGCATCAAGAACCGCATCGAGCCACACGCTCCAGTGGACAAGGACCTCTACGAACT 2093
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 CGACGGCATCAAGAACCGCATCGAGCCACACGCTCCAGTGGACAAGGACCTCTACGAACT 1320

Qy       2094 GCCACCAGAGGAAGCTGCATCCATTCCACAGGCACCAACCTCCCTGGAAGCATCCCTGAA 2153
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 ACCACCAGAGGAAGCTGCATCCATTCCACAGGCACCAACCTCCCTGGAAGCATCCCTGAA 1380

Qy       2154 GGCACTGCAGGAAGACACCGACTTCCTCACCGAGTCTGACGTCTTCACCGAGGATCTCAT 2213
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 GGCACTGCAGGAAGACACCGACTTCCTCACCGAGTCTGACGTCTTCACCGAGGATCTCAT 1440

Qy       2214 CGAGGCGTACATCCAGTACAAGTACGACAACGAGATCTCCCCAGTTCGCCTGCGCCCAAC 2273
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 CGAGGCGTACATCCAGTACAAGTACGACAACGAGATCTCCCCAGTTCGCCTGCGCCCAAC 1500

Qy       2274 CCCGCAGGAATTCGAATTGTACTTCGACTGCTAATTCACTTAGCTAGCCGATAG 2327
              |||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 CCCGCAGGAATTCGAATTGTACTTCGACTGCTAATTCACTTAGCTAGCCGATAG 1554
```

RESULT 4
ADS73713
ID ADS73713 standard; DNA; 1434 BP.
XX
AC ADS73713;
XX
DT 02-DEC-2004 (first entry)
XX
DE B. lactofermentum glnA gene nucleotide sequence.
XX
KW Coryneform bacterium; L-arginine; L-lysine; glutamine synthetase;
KW glutamine synthetase adenylyltransferase;
KW nitrogen metabolism regulation protein; arginine repressor; fermentation;
KW pharmaceutical; animal feed; glnA; gene; ds.
XX
OS Corynebacterium glutamicum.
XX
FH Key   Location/Qualifiers
FT CDS   1. .1434
FT   /*tag= a
FT   /product= "glutamine synthetase"
FT   /gene= "glnA"
FT   /note= "bacterial start codon GTG"
XX
PN EP1460128-A1.
XX
PD 22-SEP-2004.
XX
PF 02-MAR-2004; 2004EP-00004888.
XX
PR 03-MAR-2003; 2003JP-00056129.
XX
PA (AJIN) AJINMOTO CO INC.
XX
PI Matsuzaki Y, Nakamura J, Hashiguchi K;

SEQ ID NO: 2

```
Db        301 ARYYIGGILHHAGAVLAFTNATLNSYHRLVPGFEAPINLVYSQRNRSAAVRIPITGSNPK 360

Qy        361 AKRIEFRAPDPSGNPYLGFAAMMMAGLDGIKNRIEPHAPVDKDLYELPPEEAASIPQAPT 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 AKRIEFRAPDPSGNPYLGFAAMMMAGLDGIKNRIEPHAPVDKDLYELPPEEAASIPQAPT 420

Qy        421 SLEASLKALQEDTDFLTESDVFTEDLIEAYIQYKYDNEISPVRLRPTPQEFELYFDC 477
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 SLEASLKALQEDTDFLTESDVFTEDLIEAYIQYKYDNEISPVRLRPTPQEFELYFDC 477


RESULT 3
AAB79682
ID   AAB79682 standard; protein; 477 AA.
XX
AC   AAB79682;
XX
DT   30-APR-2001  (first entry)
XX
DE   Corynebacterium glutamicum MP protein sequence SEQ ID NO:98.
XX
KW   Corynebacterium glutamicum; metabolic pathway protein; MP protein;
KW   fine chemical production; microorganism; organic acid; nucleoside;
KW   nonproteinogenic amino acid; purine base; pyrimidine base; nucleotide;
KW   lipid; saturated fatty acid; unsaturated fatty acid; diol; vitamin;
KW   carbohydrate; aromatic compound; cofactor; polyketide; enzyme.
XX
OS   Corynebacterium glutamicum.
XX
PN   WO200100843-A2.
XX
PD   04-JAN-2001.
XX
PF   23-JUN-2000; 2000WO-IB000923.
XX
PR   25-JUN-1999;   99US-0141031P.
PR   01-JUL-1999;   99DE-01030476.
PR   02-JUL-1999;   99US-0142101P.
PR   08-JUL-1999;   99DE-01031415.
PR   08-JUL-1999;   99DE-01031418.
PR   08-JUL-1999;   99DE-01031419.
PR   08-JUL-1999;   99DE-01031420.
PR   08-JUL-1999;   99DE-01031424.
PR   08-JUL-1999;   99DE-01031428.
PR   08-JUL-1999;   99DE-01031434.
PR   08-JUL-1999;   99DE-01031435.
PR   08-JUL-1999;   99DE-01031443.
PR   08-JUL-1999;   99DE-01031453.
PR   08-JUL-1999;   99DE-01031457.
PR   08-JUL-1999;   99DE-01031465.
PR   08-JUL-1999;   99DE-01031478.
PR   08-JUL-1999;   99DE-01031510.
PR   08-JUL-1999;   99DE-01031541.
PR   08-JUL-1999;   99DE-01031573.
PR   08-JUL-1999;   99DE-01031592.
PR   08-JUL-1999;   99DE-01031632.
PR   08-JUL-1999;   99DE-01031634.
PR   08-JUL-1999;   99DE-01031636.
PR   09-JUL-1999;   99DE-01032125.
PR   09-JUL-1999;   99DE-01032126.
PR   09-JUL-1999;   99DE-01032130.
PR   09-JUL-1999;   99DE-01032186.
PR   09-JUL-1999;   99DE-01032206.
PR   09-JUL-1999;   99DE-01032227.
PR   09-JUL-1999;   99DE-01032228.
PR   09-JUL-1999;   99DE-01032229.
PR   09-JUL-1999;   99DE-01032230.
PR   14-JUL-1999;   99DE-01032922.
PR   14-JUL-1999;   99DE-01032926.
PR   14-JUL-1999;   99DE-01032928.
PR   14-JUL-1999;   99DE-01033004.
PR   14-JUL-1999;   99DE-01033005.
PR   14-JUL-1999;   99DE-01033006.
PR   12-AUG-1999;   99US-0148613P.
PR   27-AUG-1999;   99DE-01040764.
PR   27-AUG-1999;   99DE-01040765.
PR   27-AUG-1999;   99DE-01040766.
PR   27-AUG-1999;   99DE-01040832.
PR   31-AUG-1999;   99DE-01041378.
PR   31-AUG-1999;   99DE-01041379.
PR   31-AUG-1999;   99DE-01041380.
PR   31-AUG-1999;   99DE-01041394.
PR   31-AUG-1999;   99DE-01041396.
PR   03-SEP-1999;   99DE-01042076.
PR   03-SEP-1999;   99DE-01042077.
PR   03-SEP-1999;   99DE-01042079.
PR   03-SEP-1999;   99DE-01042086.
PR   03-SEP-1999;   99DE-01042087.
PR   03-SEP-1999;   99DE-01042088.
PR   03-SEP-1999;   99DE-01042095.
PR   03-SEP-1999;   99DE-01042124.
PR   03-SEP-1999;   99DE-01042129.
PR   09-MAR-2000; 2000US-0187970P.
XX
PA   (BADI ) BASF AG.
XX
PI   Pompejus M,  Kroeger B,  Schroeder H,  Zelder O,  Haberhauer G;
XX
DR   WPI; 2001-137957/14.
DR   N-PSDB; AAF71801.
XX
PT   Nucleic acids from Corynebacterium glutamicum encoding metabolic pathway
PT   proteins, useful for producing fine chemicals in microorganisms,
PT   including organic acids, nonproteinogenic amino acids, and purine and
PT   pyrimidine bases.
XX
PS   Claim 20; Page 303-305; 1737pp; English.
XX
CC   AAF71753 to AAF72330 encode the Corynebacterium glutamicum metabolic
CC   pathway (MP) proteins given in AAB79634 to AAB80211. The C. glutamicum MP
CC   nucleic acids are useful for the production of fine chemicals in
CC   microorganisms, including organic acids, nonproteinogenic amino acids,
CC   purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated
CC   and unsaturated fatty acids, diols, carbohydrates, aromatic compounds,
```

SEQ ID NO: 2

```
CC   vitamins, cofactors, polyketides and enzymes
XX
SQ   Sequence 477 AA;

  Query Match             99.9%;  Score 2516;  DB 4;  Length 477;
  Best Local Similarity   99.8%;  Pred. No. 5e-242;
  Matches  476;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 VAFETPEEIVKFIKDENVEFVDVRFTDLPGTEQHFSIPAASFDADTVEEGLAFDGSSIRG 60
              ||||||||||||||||||||||||||||||||||||||||||||||:||||||||||||||
Db          1 VAFETPEEIVKFIKDENVEFVDVRFTDLPGTEQHFSIPAASFDADTIEEGLAFDGSSIRG 60

Qy         61 FTTIDESDMNLLPDLGTATLDPFRKAKTLNVKFFVHDPFTREAFSRDPRNVARKAEQYLA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 FTTIDESDMNLLPDLGTATLDPFRKAKTLNVKFFVHDPFTREAFSRDPRNVARKAEQYLA 120

Qy        121 STGIADTCNFGAEAEFYLFDSVRYSTEMNSGFYEVDTEEGWWNRGKETNLDGTPNLGAKN 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 STGIADTCNFGAEAEFYLFDSVRYSTEMNSGFYEVDTEEGWWNRGKETNLDGTPNLGAKN 180

Qy        181 RVKGGYFPVAPYDQTVDVRDDMVRNLAASGFALERFHHEVGGGQQEINYRFNTMLHAADD 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 RVKGGYFPVAPYDQTVDVRDDMVRNLAASGFALERFHHEVGGGQQEINYRFNTMLHAADD 240

Qy        241 IQTFKYIIKNTARLHGKAATFMPKPLAGDNGSGMHAHQSLWKDGKPLFHDESGYAGLSDI 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 IQTFKYIIKNTARLHGKAATFMPKPLAGDNGSGMHAHQSLWKDGKPLFHDESGYAGLSDI 300

Qy        301 ARYYIGGILHHAGAVLAFTNATLNSYHRLVPGFEAPINLVYSQRNRSAAVRIPITGSNPK 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 ARYYIGGILHHAGAVLAFTNATLNSYHRLVPGFEAPINLVYSQRNRSAAVRIPITGSNPK 360

Qy        361 AKRIEFRAPDPSGNPYLGFAAMMMAGLDGIKNRIEPHAPVDKDLYELPPEEAASIPQAPT 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 AKRIEFRAPDPSGNPYLGFAAMMMAGLDGIKNRIEPHAPVDKDLYELPPEEAASIPQAPT 420

Qy        421 SLEASLKALQEDTDFLTESDVFTEDLIEAYIQYKYDNEISPVRLRPTPQEFELYFDC 477
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 SLEASLKALQEDTDFLTESDVFTEDLIEAYIQYKYDNEISPVRLRPTPQEFELYFDC 477


RESULT 4
AAG93231
ID   AAG93231 standard; protein; 477 AA.
XX
AC   AAG93231;
XX
DT   26-SEP-2001  (first entry)
XX
DE   C glutamicum protein fragment SEQ ID NO: 6985.
XX
KW   Coryneform bacterium; amino acid synthesis; vitamin; saccharide;
KW   organic acid synthesis.
XX
OS   Corynebacterium glutamicum.
XX
PN   EP1108790-A2.
```

SEQ ID NO:4

```
Db        181 DRVLAESELAGADRNLSIAHMLRNYGVIEDEAHDAVLSYTLQCAIKVTTRDLAVMTATLA 240

Qy        241 AGGTHPITGKKLLDARVCRLTLSVMASAGMYDEAGQWLSTVGIPAKSGVAGGLIGILPGQ 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AGGTHPITGKKLLDARVCRLTLSVMASAGMYDEAGQWLSTVGIPAKSGVAGGLIGILPGQ 300

Qy        301 LGIATFSPRLNPKGNSVRGVKIFKQLSDDMGLHLMSTEQVSGHAVRSITRDGDTTFIQMQ 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 LGIATFSPRLNPKGNSVRGVKIFKQLSDDMGLHLMSTEQVSGHAVRSITRDGDTTFIQMQ 360

Qy        361 GAMNFSASESFLHAIVEHNFEGTEVVLDLTRVLSFHPVAIRMIKEGLKRIRDAGFEVFIL 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 GAMNFSASESFLHAIVEHNFEGTEVVLDLTRVLSFHPVAIRMIKEGLKRIRDAGFEVFIL 420

Qy        421 DPDDVLPDFMFSDGTICKERV 441
              |||||||||||||||||||||
Db        421 DPDDVLPDFMFSDGTICKERV 441
```

RESULT 2
ADD13591
ID ADD13591 standard; protein; 446 AA.
XX
AC ADD13591;
XX
DT 01-JAN-2004 (first entry)
XX
DE C. glutamicum metabolic pathway protein RXA04228.
XX
KW metabolic pathway regulation; fine chemical; lysine; nucleotide;
KW nucleoside; lipid; fatty acid; diol; carbohydrate; aromatic compound;
KW vitamin; co-factor; enzyme; food; animal feed; cosmetic; pharmaceutical.
XX
OS Corynebacterium glutamicum.
XX
FH Key   Location/Qualifiers
FT Misc-difference 279
FT   /note= "Optionally substituted with Thr"
XX
PN WO2003040681-A2.
XX
PD 15-MAY-2003.
XX
PF 31-OCT-2002; 2002WO-EP012141.
XX
PR 05-NOV-2001; 2001DE-01054292.
XX
PA (BADI) BASF AG.
XX
PI Zelder O, Pompejus M, Schroeder H, Kroeger B, Klopprogge C;
PI Haberhauer G;
XX
DR WPI; 2003-482273/45.
DR N-PSDB; ADD13590.
XX
PT New nucleic acid encoding variant forms of metabolic regulatory proteins,
PT useful for production of fine chemicals, specifically lysine, in
PT microorganisms.
XX
PS Claim 1; SEQ ID NO 158; 328pp; German.
XX
CC This invention describes novel Corynebacterium glutamicum
CC polynucleotides, polypeptides and variants associated with the regulation
CC of metabolic pathways. The products of the invention are used for
CC production of fine chemicals, preferably amino acids and specifically
CC lysine, but more generally nucleotides, nucleosides, lipids, fatty acids,
CC diols, carbohydrates, aromatic compounds, vitamins, co-factors and
CC enzymes, useful in the food, animal feed, cosmetics and pharmaceutical
CC industries. The polynucleotides of the invention, optionally as primers
CC and probes, can also be used for identification and classification of C.
CC glutamicum and related species, e.g. for diagnosis, for genomic mapping,
CC functional or evolutionary studies, gene manipulation and modulation of
CC metabolic activity. Cells containing the products of the invention may
CC produce fine chemicals in improved yields, with higher productivity
CC and/or more efficiently.
XX
SQ Sequence 446 AA;

```
  Query Match             98.1%;  Score 2200;  DB 7;  Length 446;
  Best Local Similarity   100.0%;  Pred. No. 2.5e-197;
  Matches  433;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          9 PQNLSCTRVYSAKEITSLDSMLTMPIPEYLHEILDDVRDTTSGELADYIPELKSADPNPL 68
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         14 PQNLSCTRVYSAKEITSLDSMLTMPIPEYLHEILDDVRDTTSGELADYIPELKSADPNPL 73

Qy         69 AVALCTVNGHIYSAGDDDIEFTMQSISKPFAYALALQECGFDEVSASVALEPSGEAFNEL 128
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         74 AVALCTVNGHIYSAGDDDIEFTMQSISKPFAYALALQECGFDEVSASVALEPSGEAFNEL 133

Qy        129 SLDGENRPMNPMINAGAIAINQLINGSDSTVEDRVEKIRHYFSELAGRELTIDRVLAESE 188
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        134 SLDGENRPMNPMINAGAIAINQLINGSDSTVEDRVEKIRHYFSELAGRELTIDRVLAESE 193

Qy        189 LAGADRNLSIAHMLRNYGVIEDEAHDAVLSYTLQCAIKVTTRDLAVMTATLAAGGTHPIT 248
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        194 LAGADRNLSIAHMLRNYGVIEDEAHDAVLSYTLQCAIKVTTRDLAVMTATLAAGGTHPIT 253

Qy        249 GKKLLDARVCRLTLSVMASAGMYDEAGQWLSTVGIPAKSGVAGGLIGILPGQLGIATFSP 308
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        254 GKKLLDARVCRLTLSVMASAGMYDEAGQWLSTVGIPAKSGVAGGLIGILPGQLGIATFSP 313

Qy        309 RLNPKGNSVRGVKIFKQLSDDMGLHLMSTEQVSGHAVRSITRDGDTTFIQMQGAMNFSAS 368
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        314 RLNPKGNSVRGVKIFKQLSDDMGLHLMSTEQVSGHAVRSITRDGDTTFIQMQGAMNFSAS 373

Qy        369 ESFLHAIVEHNFEGTEVVLDLTRVLSFHPVAIRMIKEGLKRIRDAGFEVFILDPDDVLPD 428
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        374 ESFLHAIVEHNFEGTEVVLDLTRVLSFHPVAIRMIKEGLKRIRDAGFEVFILDPDDVLPD 433

Qy        429 FMFSDGTICKERV 441
              |||||||||||||
Db        434 FMFSDGTICKERV 446
```

SEQ ID NO: 4

RESULT 3
AAG92471
ID AAG92471 standard; protein; 543 AA.
XX
AC AAG92471;
XX
DT 26-SEP-2001 (first entry)
XX
DE C glutamicum protein fragment SEQ ID NO: 6225.
XX
KW Coryneform bacterium; amino acid synthesis; vitamin; saccharide;
KW organic acid synthesis.
XX
OS Corynebacterium glutamicum.
XX
PN EP1108790-A2.
XX
PD 20-JUN-2001.
XX
PF 18-DEC-2000; 2000EP-00127688.
XX
PR 16-DEC-1999; 99JP-00377484.
PR 07-APR-2000; 2000JP-00159162.
PR 03-AUG-2000; 2000JP-00280988.
XX
PA (KYOW) KYOWA HAKKO KOGYO KK.
XX
PI Nakagawa S, Mizoguchi H, Ando S, Hayashi M, Ochiai K, Yokoi H;
PI Tateishi N, Senoh A, Ikeda M, Ozaki A;
XX
DR WPI; 2001-376931/40.
DR N-PSDB; AAH67690.
XX
PT Novel polynucleotides derived from Coryneform bacteria, for identifying
PT mutation point of a gene, measuring expression of a gene, analyzing
PT expression profile or pattern of a gene and identifying homologous gene.
XX
PS Claim 17; SEQ ID NO 6225; 246pp + Sequence Listing; English.
XX
CC The present invention provides a number of nucleotide and protein
CC sequences from the Coryneform bacterium Corynebacterium glutamicum. These
CC are useful for identifying the mutation point of a gene derived from a
CC mutant of coryneform bacterium, measuring expression amount and analysing
CC the expression profile or expression pattern of a gene derived from
CC Coryneform bacterium, and identifying a homologue of a gene derived from
CC coryneform bacterium. Coryneform bacteria are useful for producing amino
CC acids, nucleic acids, vitamins, saccharides and organic acids,
CC particularly L-lysine. The present sequence is a protein described in the
CC exemplification of the invention. Note: The sequence data for this patent
CC did not form part of the printed specification, but was obtained in
CC electronic format directly from the European Patent Office
XX
SQ Sequence 543 AA;

  Query Match   98.1%; Score 2200; DB 4; Length 543;
  Best Local Similarity   100.0%; Pred. No. 3.4e-197;

  Matches 433; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   9 PQNLSCTRVYSAKEITSLDSMLTMPIPEYLHEILDDVRDTTSGELADYIPELKSADPNPL 68
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   111 PQNLSCTRVYSAKEITSLDSMLTMPIPEYLHEILDDVRDTTSGELADYIPELKSADPNPL 170

Qy   69 AVALCTVNGHIYSAGDDDIEFTMQSISKPFAYALALQECGFDEVSASVALEPSGEAFNEL 128
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   171 AVALCTVNGHIYSAGDDDIEFTMQSISKPFAYALALQECGFDEVSASVALEPSGEAFNEL 230

Qy   129 SLDGENRPMNPMINAGAIAINQLINGSDSTVEDRVEKIRHYFSELAGRELTIDRVLAESE 188
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   231 SLDGENRPMNPMINAGAIAINQLINGSDSTVEDRVEKIRHYFSELAGRELTIDRVLAESE 290

Qy   189 LAGADRNLSIAHMLRNYGVIEDEAHDAVLSYTLQCAIKVTTRDLAVMTATLAAGGTHPIT 248
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   291 LAGADRNLSIAHMLRNYGVIEDEAHDAVLSYTLQCAIKVTTRDLAVMTATLAAGGTHPIT 350

Qy   249 GKKLLDARVCRLTLSVMASAGMYDEAGQWLSTVGIPAKSGVAGGLIGILPGQLGIATFSP 308
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   351 GKKLLDARVCRLTLSVMASAGMYDEAGQWLSTVGIPAKSGVAGGLIGILPGQLGIATFSP 410

Qy   309 RLNPKGNSVRGVKIFKQLSDDMGLHLMSTEQVSGHAVRSITRDGDTTFIQMQGAMNFSAS 368
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   411 RLNPKGNSVRGVKIFKQLSDDMGLHLMSTEQVSGHAVRSITRDGDTTFIQMQGAMNFSAS 470

Qy   369 ESFLHAIVEHNFEGTEVVLDLTRVLSFHPVAIRMIKEGLKRIRDAGFEVFILDPDDVLPD 428
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   471 ESFLHAIVEHNFEGTEVVLDLTRVLSFHPVAIRMIKEGLKRIRDAGFEVFILDPDDVLPD 530

Qy   429 FMFSDGTICKERV 441
              |||||||||||||
Db   531 FMFSDGTICKERV 543

RESULT 4
AAB79685
ID AAB79685 standard; protein; 287 AA.
XX
AC AAB79685;
XX
DT 30-APR-2001 (first entry)
XX
DE Corynebacterium glutamicum MP protein sequence SEQ ID NO:104.
XX
KW Corynebacterium glutamicum; metabolic pathway protein; MP protein;
KW fine chemical production; microorganism; organic acid; nucleoside;
KW nonproteinogenic amino acid; purine base; pyrimidine base; nucleotide;
KW lipid; saturated fatty acid; unsaturated fatty acid; diol; vitamin;
KW carbohydrate; aromatic compound; cofactor; polyketide; enzyme.
XX
OS Corynebacterium glutamicum.
XX
PN WO200100843-A2.
XX
PD 04-JAN-2001.
XX

SEQ ID NO-4

PF 23-JUN-2000; 2000WO-IB000923.
XX
PR 25-JUN-1999; 99US-0141031P.
PR 01-JUL-1999; 99DE-01030476.
PR 02-JUL-1999; 99US-0142101P.
PR 08-JUL-1999; 99DE-01031415.
PR 08-JUL-1999; 99DE-01031418.
PR 08-JUL-1999; 99DE-01031419.
PR 08-JUL-1999; 99DE-01031420.
PR 08-JUL-1999; 99DE-01031424.
PR 08-JUL-1999; 99DE-01031428.
PR 08-JUL-1999; 99DE-01031434.
PR 08-JUL-1999; 99DE-01031435.
PR 08-JUL-1999; 99DE-01031443.
PR 08-JUL-1999; 99DE-01031453.
PR 08-JUL-1999; 99DE-01031457.
PR 08-JUL-1999; 99DE-01031465.
PR 08-JUL-1999; 99DE-01031478.
PR 08-JUL-1999; 99DE-01031510.
PR 08-JUL-1999; 99DE-01031541.
PR 08-JUL-1999; 99DE-01031573.
PR 08-JUL-1999; 99DE-01031592.
PR 08-JUL-1999; 99DE-01031632.
PR 08-JUL-1999; 99DE-01031634.
PR 08-JUL-1999; 99DE-01031636.
PR 09-JUL-1999; 99DE-01032125.
PR 09-JUL-1999; 99DE-01032126.
PR 09-JUL-1999; 99DE-01032130.
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XX
PA (BADI) BASF AG.
XX
PI Pompejus M, Kroeger B, Schroeder H, Zelder O, Haberhauer G;
XX
DR WPI; 2001-137957/14.
DR N-PSDB; AAF71804.
XX
PT Nucleic acids from Corynebacterium glutamicum encoding metabolic pathway
PT proteins, useful for producing fine chemicals in microorganisms,
PT including organic acids, nonproteinogenic amino acids, and purine and
PT pyrimidine bases.
XX
PS Claim 20; Page 318; 1737pp; English.
XX
CC AAF71753 to AAF72330 encode the Corynebacterium glutamicum metabolic
CC pathway (MP) proteins given in AAB79634 to AAB80211. The C. glutamicum MP
CC nucleic acids are useful for the production of fine chemicals in
CC microorganisms, including organic acids, nonproteinogenic amino acids,
CC purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated
CC and unsaturated fatty acids, diols, carbohydrates, aromatic compounds,
CC vitamins, cofactors, polyketides and enzymes
XX
SQ Sequence 287 AA;

Query Match 64.7%; Score 1452; DB 4; Length 287;
Best Local Similarity 100.0%; Pred. No. 2.4e-127;
Matches 287; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy         52 ELADYIPELKSADPNPLAVALCTVNGHIYSAGDDDIEFTMQSISKPFAYALALQECGFDE 111
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Db          1 ELADYIPELKSADPNPLAVALCTVNGHIYSAGDDDIEFTMQSISKPFAYALALQECGFDE 60

Qy        112 VSASVALEPSGEAFNELSLDGENRPMNPMINAGAIAINQLINGSDSTVEDRVEKIRHYFS 171
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Db         61 VSASVALEPSGEAFNELSLDGENRPMNPMINAGAIAINQLINGSDSTVEDRVEKIRHYFS 120

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Qy        232 LAVMTATLAAGGTHPITGKKLLDARVCRLTLSVMASAGMYDEAGQWLSTVGIPAKSGVAG 291
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Db        181 LAVMTATLAAGGTHPITGKKLLDARVCRLTLSVMASAGMYDEAGQWLSTVGIPAKSGVAG 240

Qy        292 GLIGILPGQLGIATFSPRLNPKGNSVRGVKIFKQLSDDMGLHLMSTE 338
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Db        241 GLIGILPGQLGIATFSPRLNPKGNSVRGVKIFKQLSDDMGLHLMSTE 287
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RESULT 5
AAB79684
ID AAB79684 standard; protein; 287 AA.
XX